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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,710	07/12/2001	Narasimhaswamy Manjunath	GFN- 5339DV	4467

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,710	MANJUNATH ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 26-35* is/are pending in the application.

4a) Of the above claim(s) *30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 26-29, 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 9/15/04, has been entered.

Claims 2-25 and 33 have been canceled.

Claims 1 and 26-28 have been amended.

Claim 35 has been added.

Claims 30-31 have been withdrawn from consideration as they read on the non-elected inventions and species.

Applicant's election with traverse of Group II (claims 1, 2, 4 and 26-34), drawn to methods of inhibiting T cell cytotoxicity with PSGL-specific antibodies and the species autoimmune diseases in the Election filed 3/1/04 has been acknowledged.

Claims 1, 26-29 and 32-35 are under consideration as they read on the elected invention.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 9/15/04.
The rejections of record can be found in the previous Office Action.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The previous rejection under 35 U.S.C. 112, first paragraph, enablement for any "antibody fragment" has been obviated by applicant's amended claims.

5. Claims 1, 26-29 and 32-35 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed: "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" (see claims 1 and 26) and
"determining the dose or dose range of an antibody directed to PSGL (see claim 35(a))

Applicant's amendment, filed 9/15/04, directs support to page 6, lines 8-19 and to page 34, lines 4-10 for the "additional a step of determining that a mammalian subject would benefit from inhibition of a cytotoxic T cell activity".

It is acknowledged that page 6, paragraph 2 discloses that: "One common technique to determine a therapeutically effective amount for a given patient is to administer escalating doses periodically until a meaningful patient benefit is observed by the treatment provider".

Further, it is acknowledged that page 34, lines 9-10, discloses that: "CTL suppression might be beneficial for the treatment of autoimmune diseases".

However, the specification as filed does not provide a written description or set forth the metes and bounds of the claimed "limitations".

While these sections of the specification disclose determining therapeutically effective amounts and patient benefits, as well as "CTL suppression", there is insufficient written description and guidance as to claimed methods, as currently recited. For example, page 4 does not disclose that the patient benefit is one of inhibition of a cytotoxic response but rather "a meaningful benefit which is observed by the treatment provider".

There is insufficient written description or guidance that the treatment provider is evaluating an inhibition of a cytotoxic T cell response" (e.g. versus amelioration of a disease or condition such as autoimmune disease, the elected invention). While the specification discloses the role of PSGL in generating the function of CTLs and discloses that the suppression might be beneficial for the treatment of autoimmune diseases, there is insufficient written description and guidance as to providing a separate step of "determining", as currently recited.

Also, there is insufficient written description and guidance as to "determining a dose range"

Furthermore, as pointed out below, the claimed "limitation" set forth in claim 1(a), is indefinite in that the determination is not defined by the claims; the specification does not provide a standard for ascertaining the requisite degree. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

6. The previous rejections under 35 U.S.C. § 112, second paragraph, have been obviated by applicant's amended claims.

7. Claims 1, 26-29 and 32-34 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 26-29 and 32-34 are indefinite in the recitation of "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" (see claims 1 and 26) because the determination is not defined by the claims; the specification does not provide a standard for ascertaining the requisite degree. For example, page 4 does not disclose that the patient benefit is one of inhibition of a cytotoxic response but rather "a meaningful benefit which is observed by the treatment provider". Therefore, both the "benefit" as well as what is actually being determined by the claimed method step is ambiguous and ill-defined. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 26-29 and 32-34 are rejected under 35 U.S.C. § 102(e) as being anticipated by Cummings et al. (U.S. Patent No. 6,667,036 B2) (see entire document).

Applicant's arguments filed 9/15/04 have been fully considered but are not found convincing.

Applicant argues that not only does Cummings fail to teach or suggest inhibition of cytotoxic T cell responses but also fails to teach or suggest determining a mammalian subject would benefit from inhibition of cytotoxic T cell response, as recited by the amended claims.

Applicant does acknowledge that Cummings discusses administration of an anti-PSGL antibody includes an assessment of a clinical response. However, applicant asserts that Cummings provides no teaching or suggestion of determining a mammalian subject would benefit from inhibition of cytotoxic T cell response.

However as pointed out above, the claimed limitation reciting "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" (see claims 1 and 26) is indefinite because the determination is not defined by the claims; the specification does not provide a standard for ascertaining the requisite degree. For example, page 4 does not disclose that the patient benefit is one of inhibition of a cytotoxic response but rather "a meaningful benefit which is observed by the treatment provider". Therefore, both the "benefit" as well as what is actually being determined by the claimed method step is ambiguous and ill-defined. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

Given that the claimed limitation relied upon applicant is indefinite and that page 4 of the specification appears to support "a meaningful benefit which is observed by the treatment provider", determining an assessment of a clinical response associated with the administration of anti-PSGL antibody anticipates the newly added claimed limitation of "determining".

The following of record is reiterated for applicant's convenience.

Cummings et al. teach methods of inhibiting various inflammatory conditions including rheumatoid arthritis (e.g. see column 18, paragraph 6 and column 20, paragraph 1) with antibodies that bind PSGL (see Clinical Applications on columns 18-21 and Claims, particularly Claim 1). Given that rheumatoid arthritis is an autoimmune disease, the prior art teaching of a species reads on the claimed genus. Monoclonal antibodies and fragments thereof and pharmaceutical compositions are taught as well (e.g. see column 5, paragraph 1 and columns 30-31).

Although the reference is silent about the inhibition of a cytotoxic T lymphocyte response, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not

render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Applicant's arguments are not found persuasive.

11. Claims 1, 26-29 and 32-34 are rejected under 35 U.S.C. § 102(e) as being anticipated by Larsen et al. (U.S. Patent No. 6,277,975) (see entire document).

Applicant's arguments and the examiner's rebuttal are essentially the same as that addressed above in the rejection under 35 U.S.C. § 102(e) as being anticipated by Cummings.

Further, it is noted that column 18, paragraph 2, appears to be the same or nearly the same disclosure of "effective amounts" as disclosed on page 4 of the instant specification.

"As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e. healing of chronic conditions characterized by P-selectin or E-selectin-mediated cellular adhesion or increase in rate of healing of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect whether administered in combination serially or simultaneously."

In addition, Larsen et al. teach dosage amounts (e.g. about 0.1 μg to about 100 mg per kg body weight) as well as dosages determined by the attending physician for the individual patient (e.g. see column 19, paragraph 2) as well as the properties of neutralizing antibodies (e.g. see column 20, paragraph 2)

The following of record is reiterated for applicant's convenience.

Larsen et al. teach methods of treating a variety of conditions, including inflammatory disorders and autoimmune diseases (see column 17, paragraph 1) with antibodies that neutralize PSGL, including monoclonal antibodies and antibody fragments (e.g, see column 3-4 of the Summary of the Invention and columns 9 and 19 –20 of the Detailed Description) in therapeutically effective amounts and pharmaceutical compositions (e.g. see columns 17-19).

Although the reference is silent about the inhibition of a cytotoxic T lymphocyte response, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting

a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Applicant's arguments are not found persuasive.

12. Claims 1, 26-29 and 35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. Patent No. 6,667,036 B2) AND/OR Larsen et al. (U.S. Patent No. 6,277,975) in view of Snapp et al. (Blood 91 : 154-164 (1998), Diacovo et al. (J. Exp. Med. 183: 1193- 1203 (1996), Raychaudhuri et al. (U.S. Patent No. 6,270,769 B1) and Rooney et al. (U.S. Patent No. 5[illegible],962,318)

Cummings et al. teach methods of inhibiting various inflammatory conditions including rheumatoid arthritis (e.g. see column 18, paragraph 6 and column 20, paragraph 1) with antibodies that bind PSGL (see Clinical Applications on columns 18-21 and Claims, particularly Claim 1). Given that rheumatoid arthritis is an autoimmune disease, the prior art teaching of a species reads on the claimed genus. Monoclonal antibodies and fragments thereof and pharmaceutical compositions are taught as well (e.g. see column 5, paragraph 1 and columns 30-31).

Larsen et al. teach methods of treating a variety of conditions, including inflammatory disorders and autoimmune diseases (see column 17, paragraph 1) with antibodies that neutralize PSGL, including monoclonal antibodies and antibody fragments (e.g., see column 3-4 of the Summary of the Invention and columns 9 and 19 –20 of the Detailed Description) in therapeutically effective amounts and pharmaceutical compositions (e.g. see columns 17-19).

Cummings et al. and Larsen et al. differ from the claimed methods by not disclosing "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" as a separate step.

As indicated above, there is an ambiguity as the nature and metes and bounds of this limitation in the claims. For this rejection under 35 U.S.C. § 103(a), it is noted that the recitation of "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" (e.g. see claims 1 and 26) and "determining the dose or dose range of an antibody directed to PSGL that would inhibit a cytotoxic T cell response (see claim 35).

Snapp et al. teach that all T cells, including $CD8^+$ T cells express high levels of PSGL-1 (see entire document, including Abstract; page 155, column 1, lines 1-3) and that PSGL-1 is the principal or sole ligand for P-selectin on T cells (e.g. see page 162, column 1, paragraph 3).

Diacovo et al. teach PSGL mediates P-selectin-dependent adhesion of myeloid cells, is also present on α/β T cells and may serve a similar function (see entire document, including page 1194, column 1, paragraph 1). Also, anti-PSGL-1 antibodies have been shown to completely inhibit binding of purified P-selectin to neutrophils as well as to peripheral blood T lymphocytes (page 1200, column 2, lines 2-5). IT appears that functional PSGL-1 may be induced during antigen-mediated naïve virgin-to-memory T cell conversion in secondary lymphoid tissue (see page 1200, column 2, lines14-17).

Therefore, Snapp et al. and Diacovo et al. teach that $CD8^+$ T cells, wherein the hallmark of said $CD8^+$ T cells is their ability as cytotoxic T lymphocytes (CTL) to kill other cells. Activated cytotoxic T lymphocytes are derived from inactive CTL precursors. CTLs are important in immunological responses, including responses to tumors and graft rejection.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Snapp et al. and Diacovo et al. to those of Cummings et al. AND/OR Larsen et al. to determine the ability of anti-PSGL-1 antibodies to modulate or inhibit the functions, including CTL functions of said $CD8^+$ T cells. Given the number and types of diseases and conditions targeted by Cummings et al. and Larsen et al., one of ordinary skill in the art would have been motivated to monitor the ability of anti-PSGL-1 antibodies to inhibit various immune responses, including the immune responses of cells expressing PSGL-1, including $CD8^+$ T cells.

Raychaudhuri et al. teach the known methods of determining CTL function (see entire document).

Rooney et al. similarly teach methods of monitoring CTL function (see entire document), including testing blocking antibodies (e.g. see column 32, paragraph 1).

Therefore, both Raychaudhuri et al. and Rooney et al. provide the known methods of testing CTL responses, including in response to immunosuppressive antibodies.

Given the teachings of the combination of references that anti-PSGL-1 inhibit a variety of immune responses and was useful in treating a number of diseases and conditions and the ability of said anti-PSGL-1 antibodies that inhibit a number of interactions and functions of targeted cells, a person of ordinary kill in the art would have been motivated to monitor the effects of anti-PSGL-1 antibodies on the targeted cells, including the $CD8^+$ T cells, in order to determine the effects of such anti-PSGL-1 treatment at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

13. Upon reconsideration that the claims of the instant application are drawn to the use of anti-PSGL-1 antibodies and the claims of copending copending application USSN 09/431,979 are drawn to the use of soluble PSGL-1, the previous provisional rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims of copending application USSN 09/431,979 has been withdrawn.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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December 27, 2004